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Short Report

The HPB controversy of the decade: 2007–2017 – Ten years of ALPPS

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ABSTRACT

Ten years ago the first patient underwent Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS). This report aimed to critically review literature on ALPPS in terms of methods, outcomes, and bias. In total, 237 English papers on ALPPS were identified, 75 (32%) were letters and 43 (18%) case-reports. Forty-nine single-center series reported a median 10 patients, with 0–69% morbidity and 0–50% mortality. The indications for ALPPS were reported in 35% and 47% reported on modifications. Twenty-three multicenter series included a median 45 patients. Some reports excluded up to 399 cases. 26% reported on the indications and 35% on ALPPS modifications. Across journals, variation in positive and negative conclusions on ALPPS was observed. Ten years of ALPPS have resulted in diverse publications with a high concern of bias. Although one randomized study has been published, a more critical approach towards retrospective methodology is needed to allow pragmatic conclusions for HPB-surgeons.

In 2007, the first patient underwent Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS) in Germany. ALPPS therefore celebrates its tenth birthday in 2017. The first report [1] was received with both enthusiasm and criticism [2–4]. The excitement peaked in a first international ALPPS meeting 2014 [5] and has resulted in over 250 published papers. But where are we after 10 years in terms of solid recommendations based on solid evidence, when should ALPPS really be considered, when is it clearly contra-indicated, and what is needed to move forward to fill current gaps in knowledge?

By inducing the rapid and extensive liver growth, ALPPS conveys a surgical advantage that renders more patients with extensive hepatic tumors eligible for complete resection as demonstrated by early comparative studies [6] and recently in the first randomized trial [7]. The rapid liver growth has sparked clinical and experimental research into the mechanisms of liver hypertrophy [8–11]. However, the new procedure resulted in many uncertainties such as considerable rates of adverse perioperative outcomes [12,13] and yet uncertain oncological outcomes.

Before ALPPS, portal vein embolization (PVE) was the standard procedure available to modulate the liver remnant. Since PVE was introduced in the 1990ies, the technique, its indications and outcomes have been well defined [14,15] and some aspects studied in randomized studies [16]. Although it is expected that a new procedure comes with uncertainties regarding its place in clinical practice and its outcomes, only limited progress in elucidating these uncertainties has been achieved in the case of ALPPS in the last 5 years.

Therefore literature of ALPPS was reviewed in term of the methods, outcomes, and bias. In addition, the conclusions on ALPPS were compared across the major surgical journals.

Heterogenous cohorts and incomplete data

A PubMed search with the abbreviated term ALPPS, its full term, and 'in situ split' in titles and abstracts, revealed 349 articles as of September 2017. Among these, 261 specifically discuss ALPPS and 237 do so in English. There is an exponential increase in published ALPPS papers over time (Fig. 1A), predominantly from European

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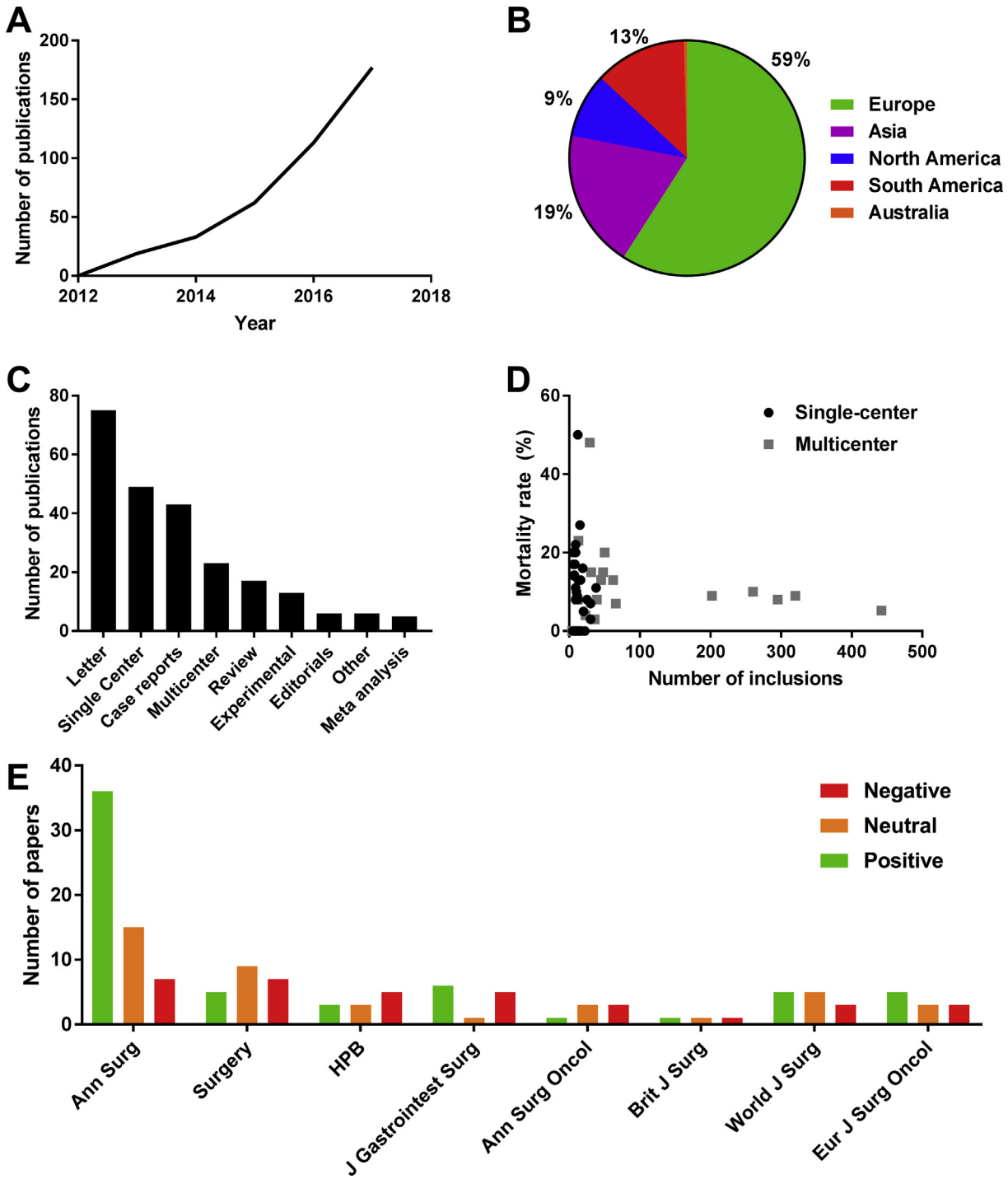

Fig. 1. **A:** Number of cumulative PubMed hits for 'associating liver partition and portal vein ligation for stages hepatectomy' (ALPPS) per year of publication. **B:** Region of origin of the first author of the PubMed articles on ALPPS. **C:** Types of articles on ALPPS in PubMed. **D:** Mortality rates reported in the respective number of included patients in the single- and multicenter reports on ALPPS. **E:** Number of opinion pieces (original contributions, commentaries, letters and editorials) in 8 leading surgical journals, classified by the authors as (positive, green) promoting ALPPS, (negative, red) critical of ALPPS or (neutral, orange) neutral towards the topic.

centers, while North American Centers have interestingly been very reluctant to adopt the innovation (Fig. 1B). Many of these papers are letters to the editor and opinion pieces, and many others are case reports, often with limited significance (Fig. 1C).

A total of 49 single center series reporting on a median of 10 (range 5–43) patients per paper were published. The majority (51%) of these single center series included multiple tumor types, resulting in small and heterogeneous series. This heterogeneity is reflected in the reported perioperative mortality rates that range from 0% to 50%, and morbidity ranging from 0% to 69%. A funnel-like convergence can be seen to a mortality rate of around 10% (Fig. 1D). The indications for using ALPPS were reported in only 35% of these single center papers. To add more to the confusion, the label "ALPPS" does not always contain ALPPS inside. Modifications of the ALPPS technique result in a plethora of new acronyms or initialism like RALPPS [17], ALPTS [18], hybrid ALPPS [19], mini-

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